2020

The Effects of Modifiable and Non-Modifiable Risk Factors on the Severity of Gastroparesis-Like Symptoms

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THE EFFECTS OF MODIFIABLE AND NON-MODIFIABLE RISK FACTORS ON THE SEVERITY OF GASTROPARESIS-LIKE SYMPTOMS

by

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A thesis submitted in partial fulfillment of the requirements
for the Honors in the Major Program in Health Sciences
in the College of Health Professions and Sciences
and in the Burnett Honors College
at the University of Central Florida
Orlando, Florida

Fall 2020

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ABSTRACT

Gastroparesis (GP) is a clinical disorder recognized by measured delayed gastric emptying without mechanical obstruction, in addition to symptoms such as nausea, vomiting, chronic abdominal pain, heartburn, early satiety upon eating a regular-sized meal, and exaggerated postprandial fullness. While GP is considered a clinically rare disorder, there is much suspicion that a much larger number of patients experience GP-like symptoms without an official diagnosis. Furthermore, little work has been done to identify the causes and exacerbations of this gastrointestinal (GI) distress in the young adult population. This study's primary goal was to establish a relationship between modifiable and non-modifiable risk factors and overall GI distress at a large university campus. Utilizing an anonymous online-based survey, risk factors (Physical, psychological, and behavioral), participant demographics, levels of perceived stress, and GI symptoms were measured from 232 participants used in our analysis. Data analysis showed several significant correlations with higher GI distress: 1) being a graduate student, 2) having a higher heart rate, 3) participating in binge drinking, and 4) having higher perceived stress levels. This study is one of the first to assess multifactorial risk factors and find significant relationships within the young adult population. These results suggest that students experiencing higher levels of perceived stress may be suffering from more debilitating GI symptoms, which supports further research into methods for mediating stress amongst the student population.

DEDICATION

To my Family: Thank you for always being my sounding board and support system throughout my entire educational journey. You have always pushed me to make each day better than the last, and the work ethic you have instilled in me has made me who I am today. You have always taught me to reach for the stars, grab hold of them, and then use them to pull myself beyond them. I promise you; I will continue to do that and make you proud. I love you.

To my Friends: You all have been my rock through some of the most tumultuous times in my life. Summer and Alex, what started as a weekend get-away turned into a momentous change in my life, which became the best years I've ever experienced. Words cannot express the gratitude, love, and appreciation I have for you both. Simply put, this could not have happened without you, and for that, I am eternally grateful for you both. To the rest of our UCF friends, new and old, thank you for bringing me into the fold and riding through these last few years with me. Although our time on campus may be coming to an end, I know we have so many more memories to make together long into the future. Thank you for giving me my home away from home and making me a part of our amazing UCF family.

To Ms. Jennifer Barreto, Ms. Brenda Treto, and the other teachers at MAST: You all were the first to put my intelligence to the test and recognize the potential that I didn't see for myself. The lessons I've learned from you have taken me further than I thought possible. You all have a stake in my success, and I will continue to use the knowledge you've passed on to make a positive change in the world and give unto others what was given to me. Myself and all of the students who have learned, or will learn under you, are some of the luckiest in the world. Thank you for all that you have done, are doing, and continue to do.

Finally, to Ms. Amy Reid and the SRI staff: You were the first to give me a chance to experience science and research all those many years ago. You pushed me far then and continue to push me now. Amy, the work you do is invaluable. I have said it before and will continue to say it: What you do changes lives. You help give students the pedestal they need to reach beyond and achieve their dreams and goals. This work would not have happened without you. FIU and SRI are beyond lucky to have you. Thank you for all that you do.

ACKNOWLEDGMENTS

My gratitude goes out to everyone who made this thesis a possibility and success. To my Thesis Chair, Dr. Danielle Webster, thank you for agreeing to take part in this project with me. I have learned so much under you, and your unwavering patience with me throughout all of it is beyond appreciated. I would not have wanted to do this with anyone else. To Dr. Jeanette Garcia, thank you for all your support and guidance throughout the entirety of this thesis. Your assistance was instrumental in the success of this project. To Dr. Katia Ferdowsi, thank you for being a resource for me to utilize whenever I needed guidance. The lessons and knowledge you have instilled in me throughout all of your courses will serve me immensely well into the future. I also want to acknowledge UCF, the department of Health Sciences, and the Burnett Honor's College for all the resources and tools made available to assist in my success. Finally, I want to acknowledge and thank all the participants who took time out of their day to partake in our project. You all are part of something that will serve the community long into the future and open new paths into future research to assist others worldwide.

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INTRODUCTION

Gastroparesis (GP) is clinically recognized as having measured delayed gastric emptying without mechanical obstruction, in addition to the presentation of hallmark symptoms such as nausea, vomiting, chronic abdominal pain, heartburn, early satiety upon eating a regular-sized meal, and exaggerated postprandial fullness (Gastroparesis Clinic, 2020). Although GP is considered a rare disease, it is estimated that many GP patients go undiagnosed due to the limitation of current diagnostic criteria (Jung, 2009). Furthermore, with the disparity of healthcare access amongst the US population continuing to be a mounting issue (Healthy People, 2020), the potential for GP patients to go undiagnosed – and therefore untreated, leading to decreased quality of life (QoL) – remains a genuine concern. As some studies estimate that gastroparesis-like symptoms may occur in a much larger percentage of the population than is physically diagnosed (Rey, 2012), it is of paramount importance to investigate the underlying factors affecting this disease.

Several studies have begun to look at the underlying causes and pathogenesis of GP. Current research has broken GP into three main subcategories based on its proposed etiology: Diabetic, Iatrogenic, and Idiopathic (Camilleri, 2013). Although Diabetic and Iatrogenic GP patients make up most cases, the remaining cases fall within the Idiopathic subgroup of patients - with no exact identifiable cause (Camilleri, 2013). Although studies have begun to determine the effects of Diabetes and post-surgical complications on GP presentation, little research has been done on the factors affecting idiopathic GP development. This limitation may, in part, be due to the small amount of clinically diagnosed patients with the disorder.

Little research has been done on comorbidities and factors that may exacerbate the symptoms of GP patients. A review of several studies has shown that stress may play a role in the

severity of GP symptoms. One study found that when rats were subjected to chronic stress levels, their gastric emptying levels were significantly delayed up to 24 hour time points (Ochi, 2008). Another study focused on the association of GP symptoms with global fatigue levels and found that GP patients with higher-rated levels of global fatigue scored more severely on the Gastroparesis Cardinal Symptom Index (GCSI) – the rating system used by healthcare providers in rating the severity of GP symptoms (Cherian, 2012). This data seems to support the theory that chronic stress may play a role in the development of GP and related symptoms. However, no direct relationship between GP symptoms in humans and other modifiable and non-modifiable risk factors has been established.

With the suspicion that GP-like symptoms occur in a much larger percentage of the population, it is clear that work is needed to identify further the causes and exacerbations of GP symptoms (Rey, 2012). In addition to furthering the medical community's knowledge of an otherwise understudied disease, it is hoped that patients who suffer from GP-like symptoms will be able to use this information to initiate specific treatment plans to control their risk factors. This study's primary goal is to establish a relationship between modifiable and non-modifiable risk factors and overall GP-like symptom severity. It is hypothesized that various risk factors, such as perceived stress levels, will play a significant role in the exacerbation of GP-like symptom presentation.

LITERATURE REVIEW

Introduction

Gastroparesis (GP) is a rare disorder affecting up to an estimated 4% of the population (Gastroparesis Clinic, 2020). The medical research regarding GP has been scarce, and little is known about the culmination and progression of GP and its symptoms. A review of current literature has shown several possible correlations between risk factors and disease presentation; however, it is clear more work is needed to understand GP in its entirety further. The following sections of this review will examine: 1) An overview of gastroparesis; 2) Non-modifiable risk factors associated with gastroparesis; 3) Modifiable risk factors; and 4) Other chronic conditions shown to play a role in gastroparesis presentation and progression.

Gastroparesis

Gastroparesis syndrome is characterized by delayed gastric emptying and various hallmark clinical symptoms such as abdominal pain, nausea, vomiting, and early postprandial fullness (Camilleri, 2013). These symptoms are thought to arise due to the disruption of one or more digestive processes that take place within the stomach, with the main digestive processes affected being: fundal accommodation, gastric contractions, and secretory action of the stomach (Grover, 2019). When food enters the stomach as a bolus, the fundus of the stomach naturally expands to accommodate the increased volume of ingested material. Following this, the stomach begins to coordinate contractions of the stomach musculature to breakdown the ingested food. These contractions cause ingested material to churn and combine within the stomach and, together with gastric secretions, form chyme, which is then exited through the pylorus and into the small intestine. In gastroparesis patients, however, these processes are dysregulated, and as a result, food remains within the stomach for longer than usual (Grover, 2019). This dysregulated digestive

mechanism may lead to inflammation of the stomach lining and irritation of the early parts of the duodenum as the overly acidic chyme finally exits the stomach.

Gastroparesis is regularly broken into three main different subgroups of patients: diabetic, iatrogenic, and idiopathic (Camilleri, 2013). Diabetes Mellitus is the disorder most commonly associated with gastroparesis, and this is likely associated with Vagus nerve neuropathy that is a more common occurrence in diabetic patients (Camilleri, 2013). Additionally, hyperglycemia (a common symptom of diabetic patients) is known to initiate pyloric contractions and slow down gastric emptying rates (Camilleri, 2013). Although a definite cause of idiopathic GP has not been determined, the disease's pathophysiological mechanisms have more recently begun to come to light. A common finding of all GP patients is a loss of Interstitial Cells of Cajal (ICC) within the fundal wall of the stomach (Liu, 2016). These ICC cells are colloquially known as the "Pacemaker Cells of the Stomach," as their role is to initiate and coordinate smooth muscle contractions needed for food to be released from the stomach as chyme (Grover 2019). Understanding the pathogenesis behind GP is essential for medical researchers to understand the GP disease state better; however, it is apparent that more work is still needed to identify the causes and factors that contribute to idiopathic GP symptom development.

The diagnosis of GP is a result of both clinical symptom interpretation and quantifiable test results. An official diagnosis is made with the use of scintigraphy, more commonly known as a nuclear Gastric Emptying Study (GES), alongside the presence of gastrointestinal (GI) symptoms (Grover, 2019). GES is considered the "gold standard" for diagnosis, given its reliability in GP diagnosis and relative ease to perform (Grover, 2019). However, there is a debate amongst the medical community on the use of such a costly and exclusive tool in the sole diagnosis of the disease (Rayner, 2005). A single GES can cost upwards of $2300 for a patient without health

insurance and may deter patients from performing the testing needed to confirm their physician's suspected diagnosis (Chogle, 2013). It is clear healthcare access continues to be a mounting issue - when compared over the last decade, rates of healthcare disparity have mostly remained constant (Healthy People, 2020). As low access to healthcare continues to be a significant factor in our society's ability to pursue medical treatment, the likelihood that many patients may go undiagnosed, and therefore untreated, remains very real.

Another tool used in diagnosing and evaluating GP is the Gastroparesis Cardinal Symptom Index (GCSI) (Revicki, 2003). This questionnaire is a subset of questions taken from the Patient Assessment of Gastrointestinal Disorders Symptom Severity Index (PAGI-SYM), a clinical tool used by physicians to quantify a patient's assessment of their symptoms relating to an upper gastrointestinal disease (Revicki, 2003). GCSI is very useful in both clinical and research settings, as it allows physicians and researchers to quantify and analyze the symptoms GP patients experience objectively (Revicki, 2003). This method allows for a deeper understanding of both the individual patient's current disease state and the progression of the patient's gastrointestinal symptoms throughout the disease.

GP is considered rare in nature, with an approximate incidence rate of only six confirmed cases per 100,000 people (Jung, 2009). Although the number of new people medically diagnosed with GP is relatively low, there is high suspicion amongst the medical community that the disease's actual prevalence may be much higher (Jung, 2009). One such study found that the number of people displaying GP-like symptoms was approximately 90 times (1.8% vs. 0.02%) higher than the number of patients who had been medically diagnosed by scintigraphy (Rey, 2012). Given this grossly disproportionate ratio, it is fair to conclude that the number of patients who genuinely have GP may be much higher than what medical research has shown.

Non-Modifiable Risk Factors

Non-modifiable risk factors are not under the patient's control that may predispose a patient to a specific condition. These may include characteristics such as age, race, ethnic background, and sex. Several studies have begun to look at which physical non-modifiable risk factors may play a role in GP presentation. Although current research is limited, some findings suggest that a higher percentage of females are presenting with idiopathic GP symptoms than their male counterparts (Parkman, 2011). Currently, an estimated 80% of all GP cases are females; however, the underlying cause of this disproportionate ratio has not been studied (Parkman, 2011). It is hypothesized that female gastric motility rates may be naturally lower than males due to the biological mechanisms of female sex hormones, leading to a higher predisposition for females to present symptomatically (Gangula, 2011).

Current research also indicates a disproportionate number of African-American patients presenting with diabetic GP (Parkman, 2011). In one such study, it was found that of patients listed in the Gastroparesis Registry, African-American patients suffered from diabetic GP at over twice the rate of their Non-black counterparts (Parkman, 2011). While the exact pathophysiological mechanism for this has not been elucidated, research has shown that African-Americans are diagnosed with diabetes mellitus at one of the highest rates of any racial group (Spanakis, 2014). However, it is worth noting that Native-Americans are thought to contract Diabetes at almost three times the rate of Black patients (Spanakis, 2014) – yet the same study found that only 3% of registered GP cases were patients of Native-American descent (Parkman, 2011). While the diagnosis rate for Diabetes may be a factor for the number of black patients experiencing GP symptoms compared to non-black patients, more work must be done to understand what other non-modifiable factors play a role in GP symptom presentation.

Modifiable Risk Factors

Much like non-modifiable risk factors, modifiable risk factors are characteristics that increase a person's likelihood of developing a specific condition. However, these factors remain under the patient's control and can change throughout their lifetime. Examples of these factors may be smoking habits, weight, diet, and psychosocial stress levels. One recurrent aspect studied in-depth in recent years is the relationship between stress and the presentation of physical illnesses. Many studies have shown a link between different stress levels and an overall modulation of immune-system function, leading to various health detriments and diseases (Salleh, 2008). On the topic of GP, early studies have shown that stress levels may be a significant factor in the presentation of symptoms. One such study in rats found that exposure to chronic stress levels seemed to slow gastric emptying rates when measured at a 24 hour time point (Ochi, 2008). While this research has helped show the possible relationship between stress and GP symptoms, more work must be done to show the effects of stress on the GI system in the human population.

In the human population, stress can be quantifiably measured through the use of a PSS or Perceived Stress Scale (PSS). A patient may use this PSS to relate their stress levels in terms of how likely it is to cause them distress and discomfort (Cohen, 1994). A PSS can also be used to determine how an individual is expected to respond to their stressors and gives the interpreter an insight into how overall effect stress is expected to affect that individual (Cohen, 1994). This tool has shown to be very useful in predicting the relationship between an individual's stress levels and the likelihood of a negative or unwanted outcome (Cole, 1999).

Another significant modifiable risk factor associated with GP symptom presentation is BMI (Boaz, 2011). Although it may be expected that patients who suffer from GP would naturally have a lower BMI or weight due to the nature of symptoms GP presents with (e.g., persistent nausea, vomiting,

etc.), the opposite is often true. Some studies indicate a correlation between obesity and a GP diagnosis, showing that obese patients may report more symptoms characteristic of gastroparesis compared to those with an average BMI level (Boaz, 2011). This correlation is not entirely surprising, given that obesity is associated with higher rates of Type 2 Diabetes, which has a known association with GP presentation. While these findings are useful in the context of diabetic GP presentation, more research needs to be done on which modifiable risks may play a role in idiopathic GP development and severity.

Associated Medical Conditions

As previously stated, the primary GP-associated chronic condition is Diabetes Mellitus (Krishnasamy, 2018). Studies have continuously shown a correlation between Diabetes and delayed gastric emptying, with up to 65% of Type 1 Diabetics and 30% of Type 2 Diabetics showing markedly decreased gastric motility (Krishnasamy, 2018). There have been several proposed theories for this association. One of the central hypotheses is that chronic hyperglycemia leads to denervation of the vagal nerve pathways responsible for the stomach's smooth muscle contractions (Krishnasamy, 2018). More recently, researchers have also found that levels of neuronal nitric oxide synthase (nNOS) enzymes are decreased amongst diabetic and idiopathic GP patients. This reduction in enzyme levels has been associated with reduced levels of ICC cells within the fundal wall of the stomach (Krishnasamy, 2018). The research regarding this is relatively recent, and more work must be done to understand the specific underlying pathogenesis of gastroparesis better. Still, it seems that multiple compounding dysregulations may lead to the symptomatic presentation of the disease.

In non-diabetic patients, it is not clearly understood what culminating factors lead to gastroparesis' symptomatic presentation, but several conditions have been linked with higher rates of GP. Of

these, the most notable are: chronic pancreatitis, end-stage renal disease, chronic pain syndrome, and systemic lupus erythematosus (Nassar, 2018). While the underlying mechanisms for these relationships have not been directly elucidated, this information is useful for physicians when considering the clinical factors in patients presenting with GP-like symptoms. It may be that the same autonomic pathways that are dysregulated in these disease states also play a role in GP development, but more research must be done to study this further.

Conclusion

While research on gastroparesis syndrome has been gaining attention in recent years, much more work is needed to understand the disease state and driving mechanisms behind GP thoroughly. While past research has begun to show the cellular mechanisms and chemical pathogenesis by which delayed gastric emptying may occur, little research has been done on the specific comorbidities and correlated stress levels that contribute to disease presentation and symptom severity. This study aims to close this gap and elucidate what specific comorbidities, perceived stress levels, and physical, psychological, and behavioral lifestyle factors may affect GP-like symptom presentation and severity.

MATERIALS AND METHODS

Study Design and Sample

College students were recruited from the University of Central Florida (UCF) to participate in this cross-sectional online study. To be eligible for the current study, individuals must have met the following criteria: 1) Be at least 18 years of age; and 2) Be enrolled in classes at the University of Central Florida. All full-time and part-time student populations were eligible, including Undergraduate, Graduate, Professional, and Non-Degree Seeking students.

Recruitment

This study was submitted for review through the University of Central Florida Institutional Review Board for approval before data collection began. Due to the anonymous nature of the collected data, this study was exempt from IRB regulation and approval. Please refer to Appendix A for a copy of the exemption letter. Students were primarily recruited via email recruitment and social media to reach a wider variety of student participants. Upon accessing the survey, students were prompted with an invitation to participate, explaining the purpose of the study and other pertinent information regarding data collection and organizer contact information.

Study Procedures

Once participants have consented to the study, they were automatically directed to the start of the study survey. This survey consisted of several demographic, psychosocial, and physical health questions in a multiple-choice or short response format. All items were presented via Qualtrics with an estimated completion time of no longer than 15-20 minutes.

Measures

Perceived Stress Scale

Perceived stress was measured using the Perceived Stress Scale (Cohen, 1994), a 10-item survey that measures the amount of stress felt during the past 30 days for a series of situations. Participants were asked to score their responses using a numerical 0 to 4 scale [0= Never, 1= Almost Never, 2= Sometimes, 3= Fairly Often, 4= Very Often]. Responses are scored by reversing the scoring (4=0, 3=1, 2=3, 1=3, 0=4) of all positively associated question-items (PSS Question #s 4, 5, 7, & 8) and then summing across all items (Cohen, 1994). Higher summation values are associated with higher levels of perceived stress. (Cohen, 1994)

GCSI

For the assessment of gastrointestinal symptom severity, the Gastroparesis Cardinal Symptom Index (GCSI) (Revicki, 2003) was utilized. The GCSI is a subset of 9-questions derivatized from the Patient Assessment of Gastrointestinal Disorders Symptom Severity Index (PAGI-SYM). Questions are broken into three subgroups to assess different symptom categories: 1) Nausea/Vomiting, consisting of three questions; 2) Post-Prandial Fullness, composed of four questions; and 3) Bloating, consisting of two questions. Participants were asked to rate the presence of their symptoms from the last 30 days using a numerical rating scale from 0 to 5 [0= Did not experience symptom in the previous 30 days, 1= Very Mild, 2= Mild, 3= Moderate, 4= Severe, 5= Very Severe], with higher scores indicative of greater symptoms of GI distress. The responses to questions in each subset can then be averaged to determine the severity of the particular symptom category. The average of each subset score can be taken to determine the overall disease burden and symptom severity (Revicki, 2003).

Risk Factor and Comorbidity Assessment

To determine the presence of health-related risk factors and comorbidities, study participants were asked to answer questions relating to health in three subsets: Physical Factors, Psychological Factors, and Behavioral Factors. Questions were adapted from the National Health and Nutrition Examination Survey (NHANES) (National Center for Health Statistics, 2020). For the assessment of physical factors, participants were asked to input data related to their physical state of health, including but not limited to: Height, Weight, Blood Pressure, and the presence of diagnosed physical health conditions. Questions regarding height, weight, and the presence of a health condition were short-response format, with all remaining items being of multiple-choice format. Participants had the option to select "Not sure" if they were unable to provide an answer to a question.

For the assessment of psychological factors, participants were asked about the presence of any current or past psychological conditions such as Anxiety Disorders and Mood Disorders. All questions within this subset were open short-response format.

For the assessment of behavioral factors, participants were asked various questions regarding personal and social behaviors over the last 30 days. Questions regarding behaviors include the use of tobacco, alcohol, and vaping devices, screen time usage, recreational and prescription drug use, average weekly exercise, water and caffeine consumption, working habits, and average sleep achievement. Questions regarding screen time usage, over-the-counter and prescription medication usage, and recreational drug use were open in short-response format. All other remaining items were in multiple-choice format.

Data Analysis

Symptom severity scores and demographics/risk factors were processed quantitatively and analyzed using Statistical Analysis Software (SAS). Primary data analysis consisted of a correlational analysis to determine significance (P-value ≤ 0.05) between variable relationships. Following the determination of any significant values, a regression analysis was carried out to determine the primary influencing factors associated with higher levels of symptom severity in our population. For analytical purposes, we collapsed the following variables into a dichotomous variable: physical activity (recommendations met or did not meet), screen time (recommendations met or not met), and education (graduate student vs. undergraduate student).

RESULTS

Participant Characteristics

A total of 232 students completed the survey and were included in the analysis. Table 1 displays the demographic characteristics of the sample. Approximately 89% of the sample were female, and 72% of the sample was White. The average age of participants was 20.8 ± 2.5, and the average BMI of the sample was 24.93 ± 6.08. Table 1 displays a breakdown of relevant participant characteristics.

Regression Model: Demographic Variables

The initial model included only demographic variables (age, sex, race, income, school level, living arrangement). Only being an undergraduate student compared to a graduate student was associated with lower GI symptom scores [β(SE)= -6.43 (2.3), p=0.0057]. The overall model was significant (p<0.0426) and accounted for 8.9% of the total variance attributed to GI scores. Table 2 displays the results of the regression model. Table 2 shows this model.

Regression Model: Demographic Variables + Health Factors

Both physical (BMI, heart rate, blood pressure, cholesterol levels, thyroid levels, HgA1C, chronic disease diagnosis, prescribed medication usage, over the counter medication usage) and psychological health (depression, anxiety, mood disorders) factors were entered into the model, along with school level. Only having a higher heart rate was related to higher GI symptoms as well [β(SE)= -11.59 (5.68), p=0.04]. Additionally, school level remained significantly associated with GI symptoms as well. The overall model was significant (p=0.05) and accounted for 15.5% of the variance attributed to GI scores. Table 3 displays this model, including the significant inclusion of student level.

Regression Model: Demographic Variables + Health Factors + Behavioral Factors

Along with school level and heart rate, behavioral factors (perceived stress, binge drinking, tobacco use, vaping, exercise, sleep duration, water consumption, alcohol use, caffeine use, working habits, electronic screen time use, drug use)It was found that participating in binge drinking [β(SE)= 3.02 (1.43), p=.036], and having higher perceived stress [β(SE)= 0.75 (0.087), p<0.0001] were associated with higher GI scores. Both having a higher heart rate [β(SE)= -11.59 (5.68), p=.04], and school-level [β(SE)= -5.93 (2.3), p=.01 remained significant. The overall model was significant (p<0.0001) and accounted for 38% of the total variance attributed to GI scores. Table 4 displays the regression model for all behavioral risk factors and the significant variables for student level and heart rate. Table 5 displays the final regression model of the final significant findings.

DISCUSSION

The purpose of this study was to examine the relationships between various physical, psychological, and behavioral risk factors with self-reported GI symptoms using the GCSI scale. From the final model of our regression analysis, the most significant relationship observed was between perceived stress scores (PSS) and gastrointestinal symptoms ($P < 0.0001$). This relationship was determined to account for approximately 20% of the sample's overall variance, indicative that perceived stress may be a driving force behind overall GI symptomology and presentation. Other significant factors associated with GI symptoms were found between educational level and GI symptoms (graduate students reporting higher GI symptoms than undergraduates), reported binge drinking, and higher heart rate levels. When perceived stress, binge drinking, heart rate, and education level were entered into the final mode, 38% of the variance attributed to GI symptoms was accounted for in this final model.

The relationship between PSS and GI symptoms is consistent with previous research, which demonstrated a link between greater perceived stress levels and GI symptoms in their population (Wilson, 2018). Prior research, which targeted a population of runners, had shown a positive relationship between increased exertion and GI distress during exercise; however, our findings did not establish a significant relationship between exercise and GI distress (Wilson, 2019). Balmus et al. also found that being a female and being older were positively associated with GI distress, but our findings did not observe this relationship (Balmus, 2019). Our study's lack of this finding may be due to our sample population being mostly female and one targeted age group of college-age students. Knowing that previous research has shown that college years are a period of increased stress for many young adults, it makes sense that these students may report higher levels of perceived stress compared to other populations (Benton et al., 2003).

These uniquely elevated stress levels may be the driving force for higher levels of GI symptoms, as shown in this study and prior research (Balmus, 2019). These findings are also consistent with research done on the role of stress and GI health, better known as the Brain-Gut-Axis, which has exhibited physiological changes within the GI system in response to increased stress levels (Mertz, 2017).

The significant relationship between graduate students and increased symptom presentation may be explained by the idea that graduate students experience higher perceived stress levels than their undergraduate counterparts. This idea has been studied previously, with increased stress levels being reported by graduate students compared to undergraduates (Geng et al., 2016). As stated in prior research, this increased stress may be due to the pressure of entering into a new part of the student's career and an increased work demand (Geng et al., 2016). This prior research is supported by our findings and highlights a need to investigate the stressors of higher education students and methods to mediate increased stress levels and GI distress.

Increases in stress levels may also explain the relationship between binge drinking and increased GCSI scores. Grzywacz et al. have previously elucidated the relationship between stress levels and the prevalence of binge drinking, finding that binge drinking increased as the number of perceived stressful events within the participant's day increased (Grzywacz, 2008). Knowing this relationship alongside our finding that perceived stress may be an indicator of GI symptoms, it makes sense that those who report higher levels of binge drinking may report worse GI symptoms or perceived stress levels. This finding may also be attributed to the physiological effects of alcohol intake on the GI system. Alcohol has been shown to contribute to various adverse physiological effects on the GI system, including inflammation of mucosal linings, muscular activity impairment, and GI secretion impairment (Bode, 1997). These impairments

alone may be a driving force for this relationship, but that cannot be effectively determined given this study's design.

The relationship between increasing heart rates and increasing GI symptoms has been demonstrated in prior research. Previous research has shown that chronic stress levels are associated with higher levels of cardiac arrhythmias, which could help explain this variation in self-reported heart rate (Johnson, 2014). This relationship may help to explain why participants with higher levels of stress would also report higher heart rates and higher levels of GI symptoms. However, it is worth noting that a significant percentage (approximately 38%) of our sample population did not have a recent heart rate recording to report. This limitation may help explain this found relationship between increased heart rate and GI symptoms because those who may be experiencing GI discomfort would likely be those to be seen by a physician's office, and therefore have a recent heart rate recording to report.

Study Limitations and Strengths

This study contributes to the growing literature base surrounding factors associated with gastroparesis-like symptoms; however, there are several limitations to this study that must be addressed. One limit is the subjective nature of the self-report survey that may be prone to bias. Many of the participants also did not know or did not report several of their physical health measures. Another limitation is that this study was limited to one large college campus, so these results may not be generalizable to other college populations without further research. Additionally, the majority of our participants were females, with only a limited number of male respondents. The current study provides evidence to investigate the relationship between perceived stress, binge-drinking, heart rate, and education level with GI distress. Further research should be done using objective diagnostic tools, rather than self-reported measurements, in a

larger and more varied population to assess the significance of these relationships further. Research could also be performed on the use of different stress-reducing measures to decrease perceived stress, which could subsequently reduce GI distress.

Even though there are several limitations to this study design, there are several important strengths worth noting. This study is one of the first to look at GI symptom risk factors from a multifactorial approach, encompassing physical, psychological, and behavioral risk factors. This study also addresses this topic within the college student population, which has not been thoroughly studied in previous literature. This study leads the way for future investigators to objectively begin to look at many of the found relationships to determine further significance and possibly identify the physiological mechanisms behind these correlations.

CONCLUSION

This study examined the relationship between health-related risk factors and higher GI symptoms. Students from a large university campus were asked to participate in a cross-sectional online survey to assess demographics along with physical, psychological, and behavioral risk factors. Using statistical regression analysis, it was found that having a higher heart rate, being a graduate student, having higher perceived stress, and participating in binge drinking were all associated with having higher GI symptoms in our population. These results are unique in assessing multifactorial risk factors in the college student population and lays the groundwork for future studies to further investigate these relationships and the physiological mechanisms behind them.

APPENDIX A: IRB EXEMPTION LETTER

UNIVERSITY OF CENTRAL FLORIDA

Institutional Review Board
FWA00000351
IRB00001138, IRB00012110
Office of Research
12201 Research Parkway
Orlando, FL 32826-3246

EXEMPTION DETERMINATION

August 24, 2020

Dear Danielle Webster:

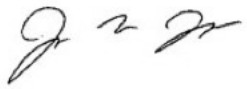
On 8/24/2020, the IRB determined the following submission to be human subjects research that is exempt from regulation:

Type of Review:	Initial Study, Category 2
Title:	The Effects of Modifiable and Non-Modifiable Risk Factors on the Severity of Gastroparesis-Like Symptoms
Investigator:	Danielle Webster
IRB ID:	STUDY00002147
Funding:	None
Grant ID:	None
Documents Reviewed:	• Explanation of Research, Category: Consent Form; • Request for Exemption, Category: IRB Protocol; • Survey Invitation, Category: Recruitment Materials; • Survey Questionaire , Category: Other;

This determination applies only to the activities described in the IRB submission and does not apply should any changes be made. If changes are made, and there are questions about whether these changes affect the exempt status of the human research, please submit a modification request to the IRB. Guidance on submitting Modifications and Administrative Check-in are detailed in the Investigator Manual (HRP-103), which can be found by navigating to the IRB Library within the IRB system. When you have completed your research, please submit a Study Closure request so that IRB records will be accurate.

If you have any questions, please contact the UCF IRB at 407-823-2901 or irb@ucf.edu. Please include your project title and IRB number in all correspondence with this office.

Sincerely,



Racine Jacques, Ph.D.
Designated Reviewer

APPENDIX B: SURVEY QUESTIONAIRE

1. Are you a currently enrolled UCF student?
    a. Yes
    b. No

2. What is your age?

3. What is your race?
    a. White
    b. Black
    c. Native American
    d. Pacific Islander
    e. Asian
    f. Other

4. What is your ethnicity?
    a. Hispanic / Latino
    b. Non-Hispanic / Non-Latino
    c. Other

5. What is your birth-sex?
    a. Male
    b. Female

6. What is your gender identity?
    a. Male
    b. Female
    c. Trans-Male
    d. Trans-Female
    e. Identity not listed/Other

7. What is your sexual orientation?
    a. Straight
    b. Gay
    c. Bisexual
    d. Sexual Orientation not listed/Other

8. What is your current level of education?
    a. Freshman
    b. Sophomore
    c. Junior
    d. Senior (4th Year)
    e. Senior (5th Year +)
    f. Graduate/Professional Student
    g. Non-Degree Seeking
9. How many people reside in your household?

10. What is your average total household income?
    a. Less than $5,000
    b. $5,000 through $11,999
    c. $12,000 through $15,999
    d. $16,000 through $24,999
    e. $25,000 through $34,999
    f. $35,000 through $49,999
    g. $50,000 through $74,999
    h. $75,000 through $99,999
    i. $100,000 or greater
    j. Not sure

When answering the following questions, think about your experiences over the *last 30 days*. Rate your experiences from 0 to 4 [0= Never, 1= Almost Never, 2= Sometimes, 3= Fairly Often, 4= Very Often]

1. How often have you been upset because of something that happened unexpectedly?
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4

2. How often have you felt that you were unable to control the important things in your life?
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4

3. How often have you felt nervous and "stressed"?
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4

4. How often have you felt confident about your ability to handle your personal problems?
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4

5. How often have you felt that things were going your way?
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4

6. How often have you found that you could not cope with all the things that you had to do?
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4

7. How often have you been able to control irritations in your life?
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4

8. How often have you felt that you were on top of things?
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4

9. How often have you been angered because of things that were outside of your control?
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4

10. How often have you felt difficulties were piling up so high that you could not overcome them?
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4

Thinking over the *last 30 days*, rate your experience with the following symptoms on a scale from 0 to 5. [0= Did not experience symptom in the last 30 days, , 1= Very Mild, 2= Mild, 3= Moderate, 4= Severe, 5= Very Severe]

1. Nausea (feeling sick to your stomach as if you were going to vomit or throw up)
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4
    f. 5

2. Retching (heaving as if to vomit, but nothing comes up)
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4
    f. 5

3. Vomiting
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4
    f. 5

4. Stomach Fullness
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4
    f. 5

5. Not able to finished a fully sized meal
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4
    f. 5

6. Feeling excessively full after meals
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4
    f. 5

7. Loss of appetite
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4
    f. 5

8. Bloating (feeling like you need to loosen your clothes)
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4
    f. 5

9. Stomach or belly visibly larger
    a. 0
    b. 1
    c. 2
    d. 3
    e. 4
    f. 5

Please enter the following measurements if you have had them collected or know their average result from the *last 30 days*. If you do not have a measurement to report, please answer "Not Sure".

1. Height

2. Weight

3. Blood Pressure
    a. Systolic < 120 **AND** Diastolic < 80
    b. Systolic 120-129 **AND** Diastolic < 80
    c. Systolic 130-139 **OR** Diastolic 80-89
    d. Systolic 140+ **OR** Diastolic 90+
    e. Systolic 180+ **OR** Diastolic 120+

f. Not Sure

4. Heart Rate (Beats per minute = BPM)
    a. < 60 BPM
    b. 60-120 BPM
    c. > 120 BPM
    d. Not Sure

5. Total Cholesterol Levels
    a. < 200
    b. 200-239
    c. > 239
    d. Not Sure

6. Thyroid Levels
    a. Diagnosed Hypothyroidism
    b. Diagnosed Hyperthyroidism
    c. Normal Thyroid Levels
    d. Not Sure

7. A1C
    a. < 5.7
    b. 5.7-6.4%
    c. 6.5%+
    d. Not Sure

8. Have you **EVER** been diagnosed with a chronic physical health condition (ex: Diabetes, Chronic Hypertension, IBS, Crohn's Disease, etc.)?
    a. Yes
        i. If yes, what condition?
    b. No

9. Have you **EVER** been diagnosed with an Anxiety Disorder (PTSD, Generalized Anxiety Disorder, Panic Disorder, etc.)?
    a. Yes
        i. If yes, what condition?
    b. No

10. Have you **EVER** been diagnosed with a Mood Disorder (Depression, Bipolar Disorder, etc.)?
    a. Yes
        i. If yes, what condition?
    b. No

11. Have you **EVER** been diagnosed with any other psychological disorder (Schizophrenia, Multiple Personality Disorder, etc.)?
    a. Yes
        i. If yes, what condition?
    b. No

12. In the PAST 30 DAYS, how many times have you smoked tobacco in the average week?
    a. 0
    b. 1-5
    c. 6-10
    d. 11-15
    e. 16-20
    f. 21+

13. In the PAST 30 DAYS, how many times have you chewed tobacco in the average week?
    a. 0
    b. 1-5
    c. 6-10
    d. 11-15
    e. 16-20
    f. 21+

14. In the PAST 30 DAYS, how many times have you used a vaping device in the average week?
    a. 0
    b. 1-5
    c. 6-10
    d. 11-15
    e. 16-20
    f. 21+

15. In the PAST 30 DAYS, how many alcoholic beverages have you consumed in the average week?
    a. 0
    b. 1-2
    c. 3-4
    d. 5-6
    e. 7+

16. In the PAST 30 DAYS, have you engaged in binge drinking? [Binge Drinking is defined as having 5+ drinks for males or 4+ drinks for females within 2 hours]
    a. Yes
    b. No

17. In the PAST 30 DAYS, how many caffeinated drinks do you consume in the average day? [Caffeinated drinks may be beverages such as coffee, tea, soda, energy drinks, etc.]
    a. 0
    b. 1-2
    c. 3-4
    d. 5-6
    e. 7+

18. In the PAST 30 DAYS, how many days do you exercise in the average week? (Exercise being defined as a moderate-intensity workout for at least 45 minutes.)
    a. 0
    b. 1-2
    c. 3-4
    d. 5+

19. In the PAST 30 DAYS, how many hours of sleep do you achieve in the average night?
    a. < 6
    b. 6-7
    c. 7-8
    d. 8-9
    e. 10+

20. In the PAST 30 DAYS, how many hours do you work in the average week?
    a. 0
    b. 1-10
    c. 10-20
    d. 20-29
    e. 30+

21. In the PAST 30 DAYS, how many hours did you typically spend on a mobile or electronic device in the average day?

22. In the PAST 30 DAYS, how many 8oz. glasses of water do you consume in the average day?
    a. 1-2
    b. 3-4
    c. 5-6
    d. 7-8
    e. 9+

23. Are you currently using any over-the-counter medications or vitamin supplements? (ex. Vitamin C, Advil, Tylenol, Aleve, etc.)
    a. Yes
        i. If yes, what type?

b. No

24. Are you currently taking any prescribed medications [**including** medically prescribed marijuana] (ex. Losartan, Metformin, Insulin, Lisinopril, Pantoprazole, etc.)?
    a. Yes
        i. If yes, what type?
        ii. If yes, for what condition?
    b. No

25. Do you currently use any recreational drugs [**NOT** including medically prescribed marijuana]?
    a. Yes
        i. If yes, what type?
        ii. If yes, how often?
    b. No

APPENDIX C: TABLES AND FIGURES

Table 1: Participant Demographics

Variable	N (%)	Mean (SD)
Age		20.8 (2.5)
Females	200 (89%)	
White	162 (72%)	
BMI		24.93 (6.08)
Undergraduates	207 (91%)	
Annual income < $25,000	40 (18%)	
Live alone	10 (4%)	

Table 2: Regression Results for Demographic Factors

Variables	β (SE)	p-value
Age	.05 (.29)	.87
White	-3.15 (3.1)	.31
Female	-3.78 (1.93)	.051
Live alone	3.81 (3.13)	.23
Income	-4.51 (3.93)	.25
School Level	-6.43 (2.3)	.0057

Table 3: Regression Results with Physical and Psychological Factors

Variables	β (SE)	p-value
BMI	.014 (.11)	.21
School Level	-5.93 (2.3)	.01
Female	-3.31 (1.97)	.09
Blood Pressure	2.04 (9.54)	.83
Heart Rate	-18.41 (7.17)	.01
Cholesterol	1.75 (2.45)	.48
Thyroid Levels	-1.35 (1.3)	.29
HgA1C	-0.53 (6.98)	.94
Anxiety Disorder	0.15 (3.27)	.96
Mood Disorder	0.42 (2.88)	.88
Other Psych Disorder	0.22 (3.39)	.94
Physical Health Dx	-3.83 (4.87)	.43

Table 4: Regression Results with Behavioral Factors

Variables	β (SE)	p-value
School Level	-5.93 (2.3)	.01
Heart Rate	-11.59 (5.68)	.04
OTC Medication	-0.82 (1.13)	.47
Prescription Medication	-0.9 (1.17)	.44
Perceived Stress Score	0.75 (0.087)	<0.0001
Screen Time	-1.3 (0.08)	.43
Vaping Habits	-1.17 (1.56)	.45
Exercise Habits	1.18 (1.68)	.48
Binge Drinking	3.02 (1.43)	.036
Caffeine Consumption	-3.58 (2.35)	.13
Hours of Sleep	1.72 (2.52)	.49
Hours of Work	-1.04 (1.61)	.51
Water Consumption	-1.15 (2.17)	.59

Table 5: Final Regression Results

Variables	β (SE)	p-value
School Level	-5.93 (2.3)	.01
Binge Drinking	3.02 (1.43)	.036
Heart Rate	-11.59 (5.68)	.04
Perceived Stress Score	0.75 (0.087)	<0.0001

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